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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/308,955	05/27/1999	KRISTIN M. LUNDY	PC9808A	6904

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EXAMINER
DELACROIX MUIRHEI, CYBILLE

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 12/31/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/308,955	Applicant(s) LUNDY et al.
	Examiner Cybille Delacroix-Muirheid	Art Unit 1614

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *June 13, 2001 and October 9, 2001* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-26* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

1. Claims 5, 6, 8, 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Berger et al., 3,896,145.

2. Claims 1, 2, 5, 6, 8, 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Holtsinger et al. or Vasseur et al.

3. Claims 3, 4, 7, 10-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Holtsinger et al. or Vasseur et al. or Berger et al, supra.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Amendment

The following is responsive to the Preliminary amendment received June 13, 2001 and the amendment received Oct. 9, 2001.

New claims 15-26 are added in the preliminary amendment received June 13, 2001. Claims 1-26 are currently pending.

The previous claims objections set forth in paragraph 3 of the office action mailed June 5, 2001 **is withdrawn** in view of the amendment received Oct. 9, 2001.

The previous claim rejection under 35 USC 112, paragraph 2, set forth in paragraph 4 of the office action mailed June 5, 2001 **is withdrawn** in view of Applicant's amendment received Oct. 9, 2001.

However, Applicant's arguments traversing the previous claims rejections under 35 USC 102(b) and 35 USC 103(a) set forth in paragraphs 5-10 of the office action mailed June 5, 2001 have been considered but are not found to be persuasive.

Said rejections are maintained essentially for the reasons given previously in the office action mailed June 5, 2001 with the following additional comment:

It is essentially Applicant's position that the prior art does not specifically use the term "cyclooxygenase" or COX-1 or COX-2 inhibitors. The claimed invention, on the other hand, characterizes the compounds of formula I as COX-2 inhibitors. Moreover, the claim language defines a selectivity ratio of COX-2:COX-1 activity inhibition based on ex vivo inhibition levels in whole blood to determine if it is at least 3:1. Applicant further explains that this ratio defines the compounds of formula I. However, the prior art does not disclose these claimed limitations.

With respect to claims 4 and 11, Applicant argues that none of the prior art discloses combining carprofen with another therapeutic compound. All the prior art relates to carprofen alone.

Said arguments have been considered but are not found to be persuasive.

Although the prior art does not specifically use the terms COX-2 or COX-1 or cyclooxygenase, the prior art continues to disclose and/or anticipate the claimed inventions because the prior art, especially Holtsinger et al. and Vasseur, disclose (1) administration of an identical compound, i.e. carprofen, to an identical host, i.e. dogs, suffering from osteoarthritis or degenerative joint disease using Applicant claimed methods steps and (2) pharmaceutical

compositions containing identical compounds which read on Applicant's claimed formula I. Furthermore, it appears that Applicant is arguing the discovery of a new property (COX-2 inhibitory activity) that is inherent to the identical compound being administered. However, it has been held that "the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to discover." Atlas Powder Co. v. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

In addressing the selectivity ratio of the claimed compounds which Applicant argues is not taught by the prior art and which defines the compounds of the instant invention, again it appears that this argument concerns the discovery of a previously unappreciated property. Yet, since both Applicant and the prior art are disclosing identical compounds, the Examiner respectfully submits that the selectivity ratio would be inherent in the compounds of the prior art.

With respect to Applicant's arguments concerning claims 4 and 11, the Examiner maintains that it would have been obvious to one of ordinary skill in the art to modify the methods and compositions of Holtsinger, Vasseur or Berger to combine an additional NSAID because Holtsinger and Vasseur teach that carprofen and other NSAID's are known in the art to be useful as analgesic, anti-inflammatory compounds. Modification to combine carprofen with the other NSAID's taught by Holtsinger and Vasseur, all of which are known to be useful for the same purpose, would have been obvious to one of ordinary skill in the art in view of the fact that the courts have held that "it is *prima facie* obvious to combine two compositions each of which is

taught by the prior art to be useful for the same purpose, in order to form a third composition which is to be used for the very same purpose" Kindly refer to In re Susi, 169 USPQ 423, 426 (CCPA 1971); In re Kerkhoven, 205 USPQ 1069 (CCPA 1980). Moreover, such a modification to combine would have been motivated by the reasoned expectation that the additive effect of the combination of carprofen and an NSAID would be successful in treating dogs suffering from degenerative joint disease or osteoarthritis.

New Ground of Rejection

Claim Objections

5. Claims 16, 19, 22 are objected to because of the following informalities: in claims 16, 19 and 22, line 4, before "oral" the term --by-- should be added. Appropriate correction is required.

6. Applicant is advised that should claim 21 be found allowable, claim 26 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claims 21 and 26 are identical in scope.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claim 15 is rejected under 35 U.S.C. 102(b) as being anticipated by Holtsinger et al. or Vasseur et al. (already of record).

Holtsinger et al. teach a method of treating dogs suffering from degenerative joint disease, the method comprising administering to the dogs an effective amount (2.2 mg/kg) of carprofen. Results show that Carprofen is effective reducing the symptoms of the joint disease. Please see the abstract; page 141, "Materials and Methods".

Vasseur et al. disclose a method of treating dogs suffering from osteoarthritis, the method comprising administering to the dogs an effective amount (2.2 mg/kg) of carprofen. Results show that the dogs responded positively to the treatment. Please see the abstract; Discussion.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 16-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Holtsinger et al. and Vasseur et al., supra.

Holtsinger et al., Vasseur et al. as applied above.

Holtsinger et al., Vasseur et al. do not specifically disclose the claimed steps of evaluating the dogs and determining whether carprofen treatment would be beneficial, nor does the prior art disclose the selective inhibition ratio of carprofen; however, it would be obvious to one of ordinary skill in the art to evaluate the dogs and determine whether treatment would be

beneficial prior to actual treatment as these are steps which are usually performed in any treatment process. Moreover, one of ordinary skill in the art would reasonably expect that the dogs undergoing treatment in Holtsinger and Vasseur were evaluated and diagnosed prior to treatment with carprofen.

Concerning the selective inhibition ratio of carprofen, since Holtsinger and Vasseur are administering an identical compound, the claimed ratio would be embraced by the compound of Holtsinger and Vasseur.

With respect to the claimed dosage amounts, since Holtsinger et al. and Vasseur et al. have established that the efficacy of the carprofen compound is dependent upon its dosage, it would have been obvious to one of ordinary skill in the art to further modify the methods and compositions of Holtsinger and Vasseur such that the carprofen is present in a dosage amount that is effective to optimize its effect on osteoarthritis or degenerative joint disease.

In addressing the claims drawn to a package, the prior art of record does not disclose a packaged pharmaceutical composition comprising carprofen along with instructional material/ printed informational material; however, modification of known pharmaceutical compositions into kits/combinations with instructional material is not novel or unobvious and is well within the capability of the skilled artisan. Furthermore, such printed material does not further limit the structural aspects of the claimed composition but only serves to inform the user of the pharmaceutical composition's intended use and/or activity.

Finally, the use of the (R) or (S)-enantiomers of carprofen would have been obvious to one of ordinary skill in the art because isomers of a racemic compound are expected to have differing activities; one isomer is expected to more active than others (optically active isomer substitution was held to be obvious). See In re Anthony, 162 USPQ 594; In re Adamson, 125 USPQ 233.

12. Claims 24-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Berger et al., 3,896,145. (Already of record).

Berger et al. teach pharmaceutical compositions useful as anti-inflammatory, analgesic and anti-rheumatic agents, the compositions comprising carbazole compounds which read on Applicant's claimed generic formula (I). The compositions are useful for oral or parenteral administration and may be in the form of tablets, capsules, suppositories, suspensions, solutions and emulsions. Please see col. 4-col. 7; col. 14, lines 1-12; col. 15, lines 8-24.

Berger et al. do not teach a pharmaceutical combination comprising the carbazole compounds and printed informational material; however, modification of known pharmaceutical compositions into kits/combinations with instructional material is not novel or unobvious and is well within the capability of the skilled artisan. Furthermore, such printed material does not further limit the structural aspects of the claimed composition but only serves to inform the user of the pharmaceutical composition's intended use and/or activity.

Finally, the use of (R) and (S)-enantiomers of the compounds would have been obvious to one of ordinary skill in the art because isomers of a racemic compound are expected to have differing activities; one isomer is expected to more active than others (optically active isomer

substitution was held to be obvious). See In re Anthony, 162 USPQ 594; In re Adamson, 125 USPQ 233.

Conclusion

Claims 1-26 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cybille Delacroix-Muirheid whose telephone number is (703) 306-3227. The examiner can normally be reached on Tue-Fri from 8:30 to 6:00. The examiner can also be reached on alternate Mondays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached on (703) 308-4725. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

CDM

Dec. 21, 2001

Cybille Delacroix-Muirheid
Patent Examiner Group 1600